Section 3

Letters sent to Local Politicians,

Deans, and JW Congregations

(Including enclosures)

ETSU
PHYSICIANS AND ASSOCIATES

325 N. STATE OF FRANKLIN ROAD
JOHNSON CITY, TENNESSEE 37604

OFFICE OF SURGERY

(423) 439-7201

Information letters regarding The PolyHeme Study were sent out to the following list of Congressmen, Senators, State Representatives and Dean of the College of Medicine @Quillen College of Medicine on October 25, 2004

Dr. Ronald Franks
William Jenkins
Matthew Hill
Bob Patton
Rusty Crowe
David Davis
Ron Ramsey

Trauma Services
Level 1 Trauma Center
Johnson City Medical Center

400 N. State of Franklin Rd
Johnson City, TN 37604

Phone: 423.431.5678
Fax: 423.431.5850

October 25, 2004

Dr. Ron Franks, Dean of Medicine
James H. Quillen College of Medicine
Box 70694
Johnson City, TN 37614

Dear Dr. Franks,

I am writing to inform you about a very important clinical study that may be conducted at Johnson City Medical Center.

Johnson City Medical Center is one of a select number of Level I trauma centers in the U.S. chosen to participate in a groundbreaking national clinical study to evaluate the safety and efficacy of PolyHeme®, an oxygen-carrying blood substitute, in increasing survival of critically injured and bleeding patients. Under the study protocol, which has been cleared for initiation by the W.S. Food and Drug Administration (FDA), treatment will begin before arrival at the hospital, either at the scene of the injury or in the ambulance, and continue during initial 12-hour post-injury period in the hospital. Since blood is not presently carried in ambulances, the use of PolyHeme® in these settings has the potential to address a critical unmet medical need by providing an oxygen-carrying solution where blood is currently not available. The study will compare the survival rate of patients receiving PolyHeme® to that of patients who receive the current standard of care, which is saline (salt water) solution.

Because the patients eligible for this study are unlikely to be able to provide prospective informed consent due to the extent and nature of their injuries, the study will be conducted under federal regulations that allow for clinical research in emergency settings using an exception from the requirement for informed consent (21 CFR 50.24).

Clinical trials at the Johnson City Medical Center are overseen by the local Institutional Review Board (IRB). The IRB is an independent body composed of medical, scientific, and nonscientific members, whose responsibility is to ensure the protection of the rights, safety, and well-being of patients enrolled in clinical trials. The traditional IRB approval of a clinical trial includes a requirement that informed consent be obtained from patients before enrollment can occur. Under the current regulations, the IRB responsible for the review, approval and continuing monitoring of a clinical trial may give approval for patient enrollment in trials in emergency situations without requiring informed consent provided specific criteria are met. The patients must be in a life-threatening situation, and the experimental therapy being evaluated must offer patients the potential for direct clinical benefit in the form of increased survival.

Before enrollment can begin, the regulations require public disclosure of information about the trial, including the potential risks and expected benefits. Consultation must also occur with representatives of the community where the study will be conducted and from which the study population will be drawn. The process is highly individualized and is tailored to the specific community and patient population involved. Our institution is beginning the process now. The purpose of this letter is to provide you with the background information in case any of your constituents contacts you regarding the study.

PolyHeme®, manufactured by Northfield Laboratories Inc. of Evanston, Illinois, is universally compatible, immediately available, oxygen carrying resuscitative fluid designed for use in urgent blood loss when blood is not immediately available. Northfield Laboratories has completed five human clinical trials over the past decade and PolyHeme® has been shown to increase survival in trials of hospitalized trauma patients compared to historical control patients who did not receive blood. In addition, Northfield is currently working with the U.S. Army on designing a Treatment IND for use of PolyHeme on the battlefield, reflecting the potential utility of PolyHeme for the military and Department of Defense.

We are excited to be included in this groundbreaking clinical study. Trauma-related injuries are a leading cause of death among Americans under 45 years old, according to the CDC's National Center for Injury Prevention and Control. In fact, almost one in five trauma patients nationally die from their injuries. We believe that if we can begin to treat these patients very early with an oxygen-carrying solution and keep their hemoglobin levels up, we might see more survivors among trauma victims in our community.

Please feel free to contact me directly should you wish to discuss this study and the implications for our community.

Sincerely yours,

Julie A. Dunn, M.D.
Principal Investigator

JAD/ash

Congregation Secretaries

Boone's Creek – Jonesborough
Charlie Blair — 2860 Carroll Creek Rd. Gray, TN 37615 — 423-753-5224

Bristol, TN
Dawson Armitage — One Monarch Drive Bristol, VA 24201 — 276-669-7640

Greeneville - East
Vincent Saylor — 270 Lincoln Dr. Greeneville, TN 37743 — 423-787-9620 423-335-5610(CELL)

Greeneville - West
Joel Bruning — 1315 Pisgah Rd. Greeneville, TN 37743 — 423-638-8360

Kingsport - West
Richard A. Sims — 571 Starlight Rd. Kingsport, TN 37664 — 423-349-7835

Elizabethton
Craig Clark — 162 Woodland Heights Elizabethton, TN 37643 — 423-543-2988 423-542-9698 (FAX) 423-895-0164 (Cell)

Johnson City - English
Barney King: — 115 E. Highland Rd. Johnson City, TN 37601 — 423-926-7841 Home 423-677-8873 Cell

Unicoi
Thomas Anderson — 210 Stephen Rd. Erwin, TN 37650 — 423-743-9503

Rogersville
Bob O'Dell — 3303 N. Hwy. 11W Surgoinsville, TN 37873-6104 — 423-345-4263

Jonesborough – Olde Towne
Frank Hartman — 122 Heritage Place Drive Jonesborough, TN 37659 — 423 753-4430

Gate City, VA
Raymond Fig — Rt. 1 Box 134 Gate City, VA 24251 — 276-452-4240

Johnson City – Spanish
Ramon Cordero — 5255 Lone Start Rd. Kingsport, TN 37660 — 423-349-4770

Trauma Services
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November 2, 2004

Dear Kingdom Hall of Jehovah's Witnesses,

Johnson City Medical Center, Washington County EMS and ETSU will be involved in a landmark clinical trail of a blood derivative called PolyHeme®. Due to the nature of this trial, we are notifying all Kingdom Halls so that they may make conscious decisions regarding their wishes to exclude themselves from this trial.

I am enclosing a PolyHeme® backgrounder to give you more in-depth explanation of the product and a copy of an insert to place in you worship bulletin. The actual start of this study will not begin until sometime in December. We will be holding at least two community meetings and then we have to go through the training process for all medical personnel involved.

If you have any questions, please feel free to contact Dr. Dunn or myself.

Sincerely,

Andrea Hyde RNBSN

Andrea S. Hyde, RN, BSN
Study Coordinator
423-439-7313 (This is a voice mail center, please leave name and number and your calls will be returned.)

NOTICE FOR HOUSE OF WORSHIP BULLETIN

Johnson City / Washington County / Jonesborough will be one of a number of communities in the U.S. in which a clinical trial evaluating an investigational product, PolyHeme®, an oxygen-carrying blood substitute, in increasing survival in severely injured and bleeding persons who are in shock will be conducted. Treatment would begin before arrival at the hospital, either at the scene of the injury or in the ambulance, and continue through a 12-hour post injury period in the hospital. Persons eligible for this trial are expected to be unable to provide consent to participate because of the nature and extent of their injuries and will be enrolled under special federal regulations providing for emergency research. For more information, please contact Julie Dunn MD, or Andrea Hyde, RN, BSN at Johnson City Medical Center, 423-439-7313.

We are distributing this notice to local houses of worship and request inclusion in your service bulletin.

Exclusion armbands will be made available to any persons wishing not to be included in this study. This study will only be for trauma victims (possibly only 1-2 per month) and will last approximately one year once the study has started.

PolyHeme® Backgrounder

PolyHeme® Characteristics

PolyHeme® is a unique human hemoglobin-based oxygen-carrying blood substitute in development for the treatment of urgent, large volume blood loss in trauma and surgical settings, with a particular focus on settings where blood is not immediately available.

PolyHeme® is the only blood substitute in development that has been rapidly and safely infused in clinical trials in sufficiently massive quantities to be useful in the treatment of urgent, large volume blood loss. PolyHeme's unique characteristics make it the ideal resuscitative fluid:

- Simultaneously restores lost blood volume and hemoglobin levels
- Is universally compatible (does not need to be typed or cross-matched before infusion)
- Is immediately available
- Supports life in the absence of red blood cells (RBCs)
- Reduces risk of disease transmission
- Does not cause transfusion reactions
- Allows rapid, massive infusion
- Has extended shelf life of over 12 months
- Is manufactured from human blood
- Has been used to treat more than 300 patients in five clinical trials.
- Favorable safety profile. No clinically significant drug-related adverse effects, specifically, no organ toxicities nor systemic or pulmonary hypertension have occurred in clinical trials to date
- In a trial of 171 trauma patients in the hospital setting, PolyHeme® significantly improved survival compared to historical controls who did not receive blood

Potential Uses for PolyHeme®

The clinical need for a safe and effective resuscitative fluid and blood substitute when blood is not available is recognized by both civilian and military trauma surgeons throughout the world. Blood may not be immediately available in the following situations:

- At the scene of injury or disaster in civilian or military settings
- During transport to the hospital via ground or air ambulance
- Upon arrival in the hospital before typing and cross-matching can be accomplished
- In the operating room in the case of unplanned surgical hemorrhage
- In remote or rural settings, including hospitals, where blood may be in limited supply
- In situations where the needs of multiple, simultaneously injured patients may overwhelm a hospital's inventory of stored blood
- In cases of inventory imbalance
- In cases of incompatibility
- In cases of religious objection
- On the battlefield

Northfield Laboratories History

Northfield Laboratories was established as a company in 1985. However, the scientific founders of Northfield began working on the development of PolyHeme® as an academic research project in 1969. At that time, the U.S. Army provided research funding to develop a blood substitute that met its criteria for utility in battlefield settings.

Northfield has always used human blood as its starting material, believing this is the most desirable starting material. PolyHeme® is derived by lysing the red blood cells in outdated human blood and extracting the tetrameric hemoglobin protein which carries oxygen from inside. Northfield's unique proprietary technology involves a chemical modification to the native hemoglobin that results in a polymerized hemoglobin molecule.

The early development of hemoglobin-based oxygen carriers (HBOCs) was problematic. Early preparations of unmodified tetrameric hemoglobin were plagued by renal, hepatic, gastrointestinal, pancreatic, and cardiovascular toxicities and resulting organ dysfunction. The small molecular-weight tetrameric species of hemoglobin have been implicated as causative agents associated with these unacceptable adverse effects. Even contemporary preparations with modified tetrameric hemoglobin have demonstrated similar evidence of such toxicities. The basis of these adverse effects has been attributed to vasoconstriction due to the small molecular-weight tetramers. The preparation of PolyHeme®, however, is designed to avoid these toxicities by removing essentially all vasoactive tetramer through high-yield polymerization and subsequent filtration to purify the solution and result in larger polymerized molecules.

Northfield has extensive experience with PolyHeme® in critically injured trauma patients, including those who have received up to 20 units or 1,000 gm of PolyHeme®. Since the normal volume of blood in a human is 10 units or 500 gm, this signifies up to 2 times the normal volume of blood in a human has been replaced successfully by PolyHeme®. Northfield has published its data showing the life-saving capability in humans following such massive blood loss, in which patients have lost virtually all of their own blood. The study was published in a manuscript entitled *The Life-Sustaining Capacity of Human Polymerized Hemoglobin when Red Cells Might Be Unavailable,* in the Journal of the American College of Surgeons in October 2002.

Civilian Ambulance Trial

Northfield is currently enrolling patients in a landmark Phase III pivotal trial using PolyHeme® starting in the prehospital setting in the field and ambulance. The trial is designed to lead to the licensure of PolyHeme® for use in trauma in both civilian and military settings. Northfield anticipates the trial will take approximately one year when underway and is hopeful that patient enrollment will begin in the late spring or early summer. Key aspects of this trial include:

- The only trial of a blood substitute in the U.S. to be conducted in the prehospital setting
- The trial will be conducted in 15-20 Level I trauma centers throughout the U.S.
- It is expected that 720 patients will be enrolled in the trial.
- The primary endpoint of the trial is survival

In the civilian environment, blood is not commonly used in the field or during ambulance transport to the hospital. The current approach to resuscitation of the trauma victim begins with the rapid infusion of salt water solution, which does not carry oxygen. PolyHeme® is a good volume replacement in lieu of salt water, and also provides immediate and universally compatible oxygen-carrying capacity.

The second stage of resuscitation is to infuse blood or red blood cells (RBCs) when they become available. In the hospital, it takes approximately 45 minutes to one hour to obtain fully cross-matched compatible blood. PolyHeme® can eliminate this delay. Therefore, PolyHeme® may represent a single initial fluid to restore both lost volume and lost oxygen-carrying capacity due to blood loss that may fundamentally alter the early care of the injured patient.

Summary

The development of PolyHeme® has progressed to the initiation of a landmark civilian ambulance trial based on the results of extensive clinical experience in critically injured trauma patients. Successful completion of this trial should lead to the licensure of PolyHeme® for use in trauma in both civilian and military settings where blood is not immediately available.

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Phone: 423.431.5678
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February 8, 2005

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I am enclosing a PolyHeme® backgrounder to give you more in-depth explanation of the product and a copy of an insert to place in you worship bulletin. The actual start of this study will not begin until sometime in March. We have held two community meetings with poor turn out and are making additional attempts to reach the community in regards to this study

If you have any questions, please feel free to contact Dr. Dunn or myself.

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Hyde, Andrea S.

From: Rburpitt@aol.com
Sent: Wednesday, February 16, 2005 4:31 PM
To: Hyde, Andrea S.
Subject: Re: Area Jehovah's Witnesses: Congregation Secretaries

Andrea, the Woodland Heights Congregation would appreciate additional "No PolyHeme" bracelets. We would be happy to make a contribution to help cover their costs. Just let me know. Please send to my address:

Robert Burpitt
381 Buckingham Rd.
Gray, TN 37615

Thanks again, Robert

Hyde, Andrea S.

From: Rburpitt@aol.com

Sent: Thursday, February 17, 2005 10:27 PM

To: Hyde, Andrea S.

Cc: tmartin10@juno.com

Subject: Re: Area Jehovah's Witnesses: Congregation Secretaries

Andrea, see my other note sent to a number of local secretaries and copied to you. I'll let you know how many bracelets are needed as soon as I hear from the secretaries. Yes, please have Northfield Labs send them to me, and I'll be happy to get them distributed.
We are sorry to cause extra work for you, and we want to do all we can to help, so please contact me at any time. We also realize the tremendous potential and importance this product has.
Warm regards, Robert D. Burpitt, Sr.
381 Buckingham Rd.
Gray, TN 37615